

FEDERAL BUREAU OF PRISONS TREATMENT GUIDELINES FOR VIRAL HEPATITIS

PURPOSE The Federal Bureau of Prisons Treatment Guidelines for Viral Hepatitis provide recommended standards for the medical management of viral hepatitis for federal inmates.

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DEFINITIONS

Hepatitis A is an acute viral hepatitis caused by a highly infectious RNA picornavirus that is transmitted primarily by the fecal-oral route. Hepatitis A has a mild to fulminant acute clinical presentation that does not progress to a chronic disease

state.

HAV is hepatitis A virus.

HAV IgM is the antibody developed against HAV during acute infection.

HAV IgG is the protective antibody developed against hepatitis A during convalescence. HAV IgG remains detectable for life and is indicative of remote infection with hepatitis A.

Hepatitis B is an acute or chronic viral hepatitis caused by a DNA virus transmitted perinatally, through blood exposure, and sexual contact. Hepatitis B has a self-limited to fulminant acute clinical presentation with approximately 10% of cases progressing to chronic hepatitis.

HBV is hepatitis B virus.

HBsAg is hepatitis B surface antigen, a viral envelope antigen that is detectable during acute or chronic hepatitis B infection and indicative of active, contagious disease.

HBV chronic carrier is a person infected with HBV with a positive serology for HBsAg for 6 months or greater.

HBc is hepatitis B core antigen, an immunogenic protein of the HBV core.

HBeAg is HBV e antigen, a secreted, viral antigen of the hepatitis B viral core that is indicative of active viral replication and increased infectiousness during acute or chronic HBV infection.

Anti-HBs is the antibody to hepatitis B surface antigen that develops during convalescence from hepatitis B. The presence of anti-HBs is indicative of remote infection with hepatitis B and usually indicates protection from recurrent or new infection with HBV.

Anti-HBc IgM is the antibody to hepatitis B core antigen that develops during the acute onset of hepatitis B, becoming undetectable 6-24 months after the onset of illness.

Anti-HBc (total) is the total antibody response to hepatitis B core antigen that develops during the onset of hepatitis B and remains detectable during convalescence. Measurement of anti-HBc is ordinarily the preferred screen for remote HBV infection.

Anti-HBe is the antibody to hepatitis e antigen that develops as viral replication and active hepatitis B begin to wane. Development of anti-HBe coincides with the loss of HBe antigen.

Hepatitis C is an acute or chronic viral hepatitis caused by a RNA virus that is transmitted primarily by parenteral contact with blood.

HCV is hepatitis C virus.

Anti-HCV is the antibody to HCV core and nonstructural proteins that is detectable from several weeks to months after clinical hepatitis. Anti-HCV is present concurrently with HCV viremia and does not confer immunity.

Anti-HCV EIA is an enzyme immunoassay used to diagnose HCV infection by measuring antibodies to HCV antigens. The presence of anti-HCV by EIA in a person with risk factors for HCV infection strongly predicts HCV infection.

Anti-HCV RIBA is the recombinant immunoblot assay that measures antibodies to the HCV antigens used in EIA through immunoblot technology. Measurement of antibodies to HCV by RIBA is used as a supplementary, "confirmatory," test for HCV infection, particularly for persons without risk factors for HCV infection who test positive for HCV antibodies by EIA.

HCV RNA assay is an assay used to qualitatively measure the presence of HCV RNA in serum. Confirming HCV viremia is necessary prior to initiating antiviral treatment of HCV infection.

HDV is hepatitis D (delta) virus, a defective RNA virus that requires HBsAg for structural integrity and replication.

Hepatitis D is an acute or chronic hepatitis caused by HDV that is transmitted primarily through injection drug usage, transfusion, or other parenteral exposures.

Delta coinfection is the simultaneous infection of HBV and HDV usually resulting in a clinical course similar to infection with HBV alone.

Delta superinfection is an acute infection of HDV with preexisting chronic HBV infection (HBsAg+), frequently exacerbating hepatitis B infection.

Anti-HDV IgM is the antibody to HDV that develops during acute delta hepatitis and recurs or persists as a marker for chronic

delta hepatitis.

Anti-HDV is the total antibody to HDV that develops following delta coinfection or superinfection. The presence of anti-HDV indicates previous infection with HDV, not necessarily active infection.

Clinician is a physician or mid-level provider.

Compensated cirrhosis is biopsy-proven cirrhosis of the liver without evidence of compromised liver synthetic function or other complications of cirrhosis.

Decompensated cirrhosis is biopsy-proven cirrhosis of the liver with evidence of compromised liver synthetic function or evidence of portal hypertension or severe liver disease, such as refractory jaundice, variceal bleeding, encephalopathy, and ascites.

Standard precautions are protective measures used for all patient/inmate contacts and situations to prevent the spread of infections transmitted by contaminated blood and body fluids. Precautions include the wearing of gloves and other personal protective equipment (personal protective equipment should be an impervious barrier) when soiling is likely; and procedures for protective handling (handling includes the use of puncture-resistant devices and leak-proof protection) of contaminated materials and equipment, and routine cleaning of all contaminated surfaces and equipment.

Absolute contraindication is a condition or factor that in and of itself ordinarily precludes a specific intervention.

Relative contraindication is a condition or factor that may preclude a specific intervention when considered in conjunction with other criteria.

PROCEDURES

Hepatitis A

1. Diagnosis

Hepatitis A should be considered as a diagnosis for any inmate presenting with symptoms of acute hepatitis, e.g. jaundice, dark urine, and diarrhea. The mean incubation period of HAV infection until the onset of symptoms is 21 days (range: 15-45 days). Hepatitis A is an acute illness, that can rarely be fulminant and life threatening, but does not evolve to a chronic infection.

Acute hepatitis A infection is confirmed by a positive serum HAV IgM that is detectable within 5 to 10 days after the onset of clinical symptoms and can persist up to 6 months after the initial infection. All inmates presenting with symptoms of acute hepatitis should be tested for the presence of HAV IgM, unless evidence of previous hepatitis A infection exists (positive HAV IgG). Routine screening for HAV infection in asymptomatic inmates is not clinically indicated or recommended by the Centers for Disease Control prior to work assignments.

2. Treatment

No specific treatment options exist for HAV infection. Treatment efforts are supportive. Fulminant hepatitis is a rare but serious complication of HAV infection, usually requiring hospitalization.

3. Prevention

Hepatitis A vaccination is a highly immunogenic, inactivated vaccine that is administered intramuscularly in the deltoid or gluteal (upper outer quadrant) muscle in a two-shot series 6-12 months apart depending on the vaccine preparation. Using the vaccine according to the licensed schedule is preferable but based on the significant immunogenicity of both available vaccines (HAVRIX: formulated with a preservative; and VAQTA: formulated without a preservative) the two brands of hepatitis A vaccine can be considered interchangeable. Vaccination of a person with previous immunity to HAV infection does not increase the risk of adverse events. Prevacination serologic screening (HAV IgG) for previous HAV infection for candidates for vaccination is cost effective for certain populations at high risk for previous HAV infection such as foreign-born inmates. Hepatitis A vaccine should not be administered to persons with hypersensitivity to alum or components of the vaccine. Hepatitis A vaccine is not routinely indicated or recommended by the Centers for Disease Control for inmates workers who are plumbers or foodworkers.

The following inmates should be considered candidates for hepatitis A vaccination:

- Inmates with chronic liver disease or cirrhosis, including HCV infection with underlying liver disease.
- Inmates with clotting-factor disorders who are administered clotting-factor concentrates (especially solvent-detergent-treated preparations).
- Inmate populations in consultation with local and state health departments, when directly affected by community-based

or prison-based hepatitis A outbreaks.

Postvaccination serologic testing for immunity is not indicated since the hepatitis A vaccine is highly efficacious.

4. Infection Control Measures

HAV is spread fecal-orally by person-to-person contact or ingestion of contaminated food or water (relatively uncommon). The virus is stable in the environment for days to several weeks and can be foodborne. Inmates diagnosed with hepatitis A infection should be considered contagious three weeks before to 10 days after the onset of jaundice. The spread of infection is greatly augmented by diarrhea. Inmates diagnosed with acute hepatitis A should be managed in accordance with the following guidelines:

- Isolated in a single cell with separate sink and toilet (e.g. medical unit, Special Housing Unit) until 10 days after the onset of jaundice and until clinically improving without diarrhea.
- Immediately removed from any assigned duties as a food handler.
- Counseled regarding the importance of strict hand washing practices.
- Managed using standard precautions to prevent fecal-oral transmission when potentially in contact with contaminated body fluids (This includes wearing of gloves or other personal protective equipment).
- Evaluated by a health care provider daily while acutely ill and during convalescence when medically indicated.

5. Contact Investigation/Post-exposure Management

Contact investigations should be coordinated with local and state health departments. If the source-case is a food handler, public health officials should be directly involved in the investigation to evaluate the risk and evidence for foodborne disease and the need for immunoprophylaxis.

The following persons are candidates for post-exposure prophylaxis for hepatitis A if exposed to the source-case during the period of contagiousness:

- cell mate(s)

- sexual contacts
- persons routinely sharing toilet facilities
- other food handlers if source-case was food handler
- very close contacts such as those who have shared eating utensils and cigarettes

Post-exposure prophylaxis is provided by passive immunization with pooled serum immunoglobulin (IG) in accordance with the following guidelines:

- Screening for antibodies to HAV is not recommended so that prophylaxis is not delayed.
- IG is administered 0.02 ml/kg intramuscularly (single dose).
- IG prophylaxis is not effective unless administered within 2 weeks of exposure.
- Persons with prior hepatitis A vaccination or previously documented natural immunity do not require passive immunization with IG.
- Hepatitis A vaccination has not been proven to prevent infection following exposure to HAV and is not indicated for post-exposure prophylaxis. Hepatitis A vaccination may be indicated for inmate populations determined to be a potential future risk of exposure in the context of an investigated outbreak. Post-vaccination antibody testing (HAV IgG) is not necessary since hepatitis A vaccine is highly efficacious.

Hepatitis B

1. Diagnosis

Routine screening of inmates for HBV infection should ordinarily be conducted in accordance with the following criteria:

- Inmates with signs or symptoms of acute or chronic hepatitis
- Asymptomatic inmates with elevated ALT levels of unknown etiology
- Inmates on chronic hemodialysis (screened every 3-4 months) who do not have natural immunity or fail to develop antibodies after vaccination

- Pregnant inmates
- Inmates with histories of percutaneous exposures to potentially infected blood, such as injection drug use or receiving tattoos or body piercings while in jail or prison
- Inmates with self-reported high risk behaviors for HBV infection.

HBV screening for asymptomatic, highly mobile, presentenced inmates in BOP detention facilities should ordinarily not be pursued unless specifically indicated for medical reasons. Asymptomatic presentenced inmates in BOP detention facilities with histories of injection drug use or other high risk behaviors for HBV infection, should be counseled regarding their risk for HBV infection and behaviors that will reduce transmission of HBV infection to others.

Acute hepatitis B: The mean incubation period of HBV infection until the onset of symptoms is 70 days (range: 30-180 days). The severity of acute hepatitis B can range from subclinical to fulminant disease with 5-10% of patients developing chronic HBV infection. Acute hepatitis B is associated with arthritis, serum sickness, rash, and myelitis. The diagnosis of acute HBV infection is suggested by the presence of HBsAg and is confirmed by the presence of anti-HBc IgM (The latter test is a necessary confirmatory test, since persons chronically antigenemic with HBsAg can be acutely infected with other pathogens that cause acute hepatitis).

Chronic hepatitis B: The diagnosis of chronic HBV infection is confirmed by the presence of HBsAg, the viral marker indicative of ongoing HBV activity and infectiousness. Infected persons may be asymptomatic. A description of commonly encountered serologic markers in chronic HBV infection include the following:

- Elevation of total anti-HBc is always present.
- HBeAg may be present and is indicative of ongoing viral replication and increased contagiousness.
- Anti-HBs is usually not detected. The presence of anti-HBs when HBsAg is also measurable does not indicate immunity or recovery from disease.
- Anti-HBe develops with the loss of HBe antigen.

2. Counseling

Inmates diagnosed with acute or chronic hepatitis B infection

should be counseled by a health care provider about the natural history of the infection, monitoring parameters, existing treatment options, and specific preventive measures for preventing transmission of HBV infection during incarceration and upon release.

3. Disease Course/Monitoring Chronic Infection

Resolution of the carrier state for chronic HBV infection (loss of HBsAg) occurs at an annual rate of approximately 1-2%. Highly infectious chronic carriers (HBe+/HBsAg+) develop anti-HBe antibodies at an annual rate of 5-10% that is associated with transient elevation in hepatocellular enzymes. The development of anti-HBe antibodies indicates a nonreplicative stage of infection. In persons in whom HBeAg disappears, the remission is usually sustained resulting in clearance of HBV DNA in the serum and resolution of liver disease. Some persons who clear HBe antigen and HBV DNA from the serum remain HBsAg+, however liver injury leading to cirrhosis does not usually occur in these individuals.

Chronic hepatitis B may be characterized by intermittent episodes of jaundice and the development of cirrhosis. Flares of hepatitis occur with delta superinfection, immunosuppressive treatments or conditions, and interferon therapy. Hepatocellular carcinoma, highly associated with HBV infection, increases in incidence with the duration of infection (median onset - 35 years). Other HBV-related conditions include polyarteritis nodosa and membranous glomerulonephritis.

A baseline physician evaluation should be conducted for all HBV chronic carriers (HBsAg+) and include:

- Targeted history and physical examination
- Serum alanine aminotransferase levels (ALT)
- Bilirubin, albumin, prothrombin time and other liver function studies if liver transaminases are elevated
- Renal function assessment
- HBeAg
- HCV antibody testing by EIA
- HIV serology if risk factors for HIV infection are identified

Periodic clinician evaluations and laboratory studies for HBV

chronic carriers should be scheduled and ordered on a case by case basis as clinically indicated depending on the severity of the inmate's liver disease and its associated complications. Inmates with nonelevated alanine aminotransferase (ALT) levels, or stable marginally elevated ALT levels should have levels remeasured every 12 months. Inmates with ALT levels greater than 1.5 times normal or with symptoms of hepatitis or other complications should be rescreened and evaluated on a more frequent basis. Screening tests for hepatocellular cancer have an unclear predictive value and are not routinely indicated. Measurement of serum alpha-fetoprotein levels and a liver ultrasound should be considered as cancer screening tests for inmates with cirrhosis.

4. Treatment

Acute Hepatitis B

Treatment of acute hepatitis B is supportive. Acute HBV infection may be subclinical, mild, or fulminant.

Chronic Hepatitis B

Alpha interferon is FDA-approved for the treatment of persons with chronic hepatitis B, providing effective therapy for a subset of carefully selected patients with sustained response rates of 30%-40%. Evaluation for alpha interferon therapy should be in accordance with Appendix 1 - Evaluation Strategy for Treatment of Chronic Hepatitis B.

Indications/considerations for treatment:

Treatment with interferon should ordinarily be considered in accordance with the following criteria:

- Chronic HBV infection (HBsAg+) documented for at least 6 to 12 months duration
- Evidence of active viral replication (HBeAg+) for 6 to 12 months
- Chronic liver inflammation documented by elevated serum alanine aminotransferase (ALT) levels at least 1.5 times greater than normal determined by averaging 3 ALT levels each measured at least one month apart over 6 to 12 months
- Absence of decompensated cirrhosis: absence of ascites, jaundice, esophageal varices or other evidence of portal hypertension or poor liver synthetic function

- Absence of absolute contraindications for interferon treatment as enumerated in Appendix 2, Contraindications to interferon and ribavirin therapy
- No evidence of active substance abuse (check urine toxicology screen if drug use suspected)
- Careful review of relative contraindications of interferon therapy

Special treatment issues:

- Alpha interferon should not be prescribed to an inmate who has only recently stopped alcohol or illicit drug use. Typically at least a 6-12 month abstinence is recommended before starting interferon therapy in nonincarcerated populations. Inmates with histories of substance abuse and hepatitis B should be referred for drug education, nonresidential drug treatment, and residential drug treatment, as appropriate and in accordance with BOP policy as a component of their treatment plan.
- Renal insufficiency secondary to glomerulonephritis from HBV infection may respond to interferon and is not in and of itself a contraindication to treatment, however interferon therapy should be considered in consultation with a specialist.
- Interferon therapy for persons with hepatitis B and hepatitis C viral co-infections is relatively contraindicated since safely monitoring the response to treatment and predicting clinical response or deterioration is difficult. Interferon/ribavirin therapy may be considered on a case by case basis in this setting after carefully weighing the benefits and risks of treatment in consultation with a specialist.
- Interferon therapy for persons with chronic hepatitis B and HIV infection or other immunosuppressive conditions is relatively contraindicated, since response rates are uncertain and drug administration may be more harmful than beneficial. Interferon therapy is ordinarily not recommended in this setting.

Clinical evaluation of inmates prior to interferon treatment:

- Inmates who are candidates for interferon should have serum HBV DNA measured to determine the **qualitative** presence of detectable HBV levels in the blood prior to initiating drug therapy. **Quantitative** HBV DNA measurements are poorly

standardized, but may be useful on a case by case basis to help predict response to treatment.

- Interferon should only be used as a treatment option for hepatitis B with an initial subspecialty consultation and follow-up subspecialty care as clinically indicated.

- Inmates with detectable levels of HBV DNA, who are otherwise candidates for interferon treatment should have a screening liver ultrasound for evidence of other liver pathology. If treatment with interferon is considered, the inmate should be referred for subspecialty evaluation and liver biopsy to confirm the diagnosis of chronic hepatitis, preclude other causes of liver disease, grade the severity of injury, and assess the degree of fibrosis. Interferon treatment should ordinarily not be initiated without a liver biopsy.

Interferon treatment should not be prescribed for persons with decompensated cirrhosis, since treatment often exacerbates disease and severe life threatening side effects have been documented.

- The evaluating physician should carefully review the inmate's medical history for absolute medication contraindications to interferon treatment and carefully weigh any relative contraindications to therapy. The benefits and toxicities of treatment should be explained to the inmate and documented in the inmate's medical record by the prescribing physician. The average response rate to interferon is 30-40%, but may be as low as 5% or less if factors that predict a favorable response are not present. Predictors of a positive response rate (30-40%) to interferon therapy for chronic hepatitis B infection include the following:

- Short duration of disease
- High aminotransferase levels (>100 U/L)
- Low HBV DNA levels (< 200 pg/mL)
- Liver necroinflammation on biopsy
- Absence of renal failure, HIV infection, or other serious co-morbidity

- Inmates should receive the following baseline evaluations prior to considering interferon therapy:

- Physician evaluation and clearance
- Psychiatrist or psychologist evaluation and clearance

- Serum ALT, albumin, bilirubin, prothrombin time, and creatinine
- CBC with differential and platelet count
- Thyroid function studies (T4/TSH)
- ANA/ferritin
- Serologic assays for HBsAg, HBeAg, and HBV DNA
- HCV antibody testing by EIA
- HIV antibody testing
- Pregnancy testing for female inmates
- Screen for delta hepatitis (anti-HDV) if from a high risk country (e.g. Italy, Middle East, Central Africa) (Delta hepatitis is treated differently than hepatitis B alone)
- Other studies/evaluations to assess the etiology of liver disease as clinically indicated and recommended by subspecialist

Administering interferon therapy:

The recommended treatment regimen for interferon alpha is 5 million units **daily** or 10 million units **thrice weekly** given subcutaneously for 16 weeks.

Treatment with interferon almost universally results in significant side effects for the patient. The prescribing physician should ensure that the inmate has a thorough understanding of the potential side effects of this therapy. An influenza-like reaction usually evolves within 6 to 8 hours of initiating treatment. This acute reaction normally abates with subsequent treatments and can be partially aborted by premedicating with antipyretics.

Chronic side effects of fatigue, myalgia, headaches, irritability, rage, confusion, and neuropsychiatric disorders can occur. Severe incapacitating depression can develop in persons without previous histories of depression. Bone marrow suppression of hematocrit, leukocyte count, and platelet count are serious effects of interferon that should be anticipated and monitored closely. Thyroiditis, hyperthyroidism, and hypothyroidism have been reported in 2.5-20 percent of persons treated and often result in irreversible thyroid dysfunction, even with cessation of drug therapy. Inmates with side effects

to interferon should have their dosage reduced or therapy discontinued depending on the severity of the side effects. Very serious sequelae occur with 2% of persons receiving interferon treatment and can include: cardiac decompensation, renal failure, pneumonitis, severe bone marrow suppression, and suicide.

Inmates should receive at least the following follow-up evaluations during treatment with interferon:

- Clinician evaluations before each injection for the first two weeks of treatment and at least biweekly thereafter (Physician evaluations at least monthly)
- Subspecialty evaluations as clinically indicated
- ALT at weeks 1,2, and 4, and at 4-8 week intervals thereafter
- Bilirubin, prothrombin time and other liver function studies with new elevations in ALT
- CBC with differential and platelet count at weeks 1, 2, and 4 and at 4-8 week intervals thereafter.
- Thyroid function studies every 3 to 6 months during therapy
- Psychiatry or psychology evaluations as clinically indicated during treatment

Transient increases in aminotransferase levels are common during therapy and correlate with immune system clearance of HBV and disappearance of HBeAg. Mild to moderate increases in liver enzymes should not be an indication for reducing or discontinuing interferon therapy, unless associated with deteriorating hepatic synthetic function or jaundice.

Monitoring response to interferon therapy of chronic hepatitis B:

The loss of HBe antigen after drug treatment predicts a favorable clinical outcome that may be sustained. Effectiveness of interferon therapy should be assessed 6 months after completion of therapy by measurement of the following parameters:

- Absence of HBeAg
- Absence of HBV DNA
- Normalization of ALT

HBeAg may not return to normal for several months after the completion of interferon treatment. HBsAg may remain positive for years after completion of effective treatment.

Other treatment options for chronic hepatitis B:

The nucleoside analogue, lamivudine has been approved by the Food and Drug Administration for the treatment of chronic hepatitis B. Lamivudine is given orally, 100 mg/day for at least 1 year, resulting in a seroconversion response in nearly one third of treated patients. Relapses are common with cessation of therapy. Response rates may increase with longer durations of therapy. In contrast to interferon, lamivudine has been effective in persons with normal ALT or low HBV DNA levels. A major limitation of lamivudine monotherapy, however, is the frequent development of lamivudine resistant, mutated HBV strains. The development of resistant strains may or may not be of long term clinical significance, but could potentially limit future treatment options in persons who relapse or do not respond to lamivudine monotherapy. Due to the evolving indications/concerns for administering lamivudine for chronic hepatitis B, this treatment option is not routinely recommended and should only be considered after consultation with a subspecialist with experience in treating patients with chronic hepatitis B.

Combination therapy of chronic hepatitis B with interferon and lamivudine has not been proven to be effective.

Steroids are not indicated for the treatment of chronic hepatitis B.

5. Infection Control Measures

Transmission: Hepatitis B virus is spread through percutaneous and mucosal exposures to infected blood and body fluids. Major modes of acquiring HBV infection include injection drug use, sexual intercourse with an infected partner, perinatal transmission from mother to child, chronic hemodialysis, and occupational exposures by health care workers. Tattooing with shared, contaminated needles or needle-like devices in jails and prisons is another potential mode of HBV transmission, specifically affecting inmate populations.

Inmates should be counseled during orientation to the institution and when appropriate during clinical evaluations of the importance of preventing blood exposures to others during activities of daily living such as sharing toothbrushes and razors and through prohibited behaviors such as sharing injection drug use equipment, tattooing, and sexual contact with other inmates. All blood exposures from other inmates, regardless of

the source, should be considered potentially contagious.

Inmates with known acute or chronic hepatitis B viral infection (HBsAg+) should be counseled on the specific measures necessary for preventing further transmission of HBV to others during incarceration and upon release and should be managed while incarcerated in accordance with the following guidelines:

- Managed using standard precautions
- Managed using infection control practices in which non-disposable patient-care items are appropriately cleaned, disinfected, or sterilized based on the use; and measures are taken to prevent cross contamination during patient care, i.e., dialysis, vascular access, cauterizing, dental procedures, etc., in accordance with Centers for Disease Control Guidelines on Handwashing and Hospital Environmental Control
- If receiving hemodialysis, HBV-infected inmates should be isolated in separate areas and when feasible, assigned units designated for HBsAg+ inmates only; **or**, scheduled separately for dialysis to prevent cross contamination between seronegative inmates, i.e., HBsAg+ inmates are dialyzed on different days or time periods than HBsAg seronegative inmates. In addition, reasonable measures should be taken to provide HBsAg+ inmates with specifically assigned chairs, medications, supplies, and staff.

6. Prevention and Post-exposure Management

Hepatitis B vaccination

Indications: Hepatitis B vaccination is routinely indicated (unless medically contraindicated) for the following inmates in accordance with BOP policy and medical indications:

- Inmate workers at risk for bloodborne pathogen exposure in accordance with the institution's exposure control plan.
- Inmates on chronic hemodialysis
- Inmates with HIV infection with risk factors for acquiring HBV infection
- Post-exposure prophylaxis for unprotected inmates following percutaneous or permucosal exposures to infected or potentially infected blood, such as tattooing, as recommended by Centers for Disease Control and Prevention guidelines

- When otherwise medically indicated on a case by case basis

Administration of vaccine: Hepatitis B vaccination should be administered in accordance with the following guidelines:

- Prevacination serologic screening for prior HBV infection (immunity) by measurement of anti-HBc or anti-HBs should be considered for inmates with risk factors for previous HBV infection, such as injection drug use.
- A previous anaphylactic reaction to baker's yeast, any vaccine component, or previous hepatitis B vaccination is a contraindication to vaccination or booster vaccination.
- Based on limited data, hepatitis B vaccine contains no components that have been shown to pose a risk to the fetus or newborn. Pregnancy should not be considered an absolute contraindication to vaccination for women at risk of acquiring HBV infection, since HBV poses a significant risk to the fetus or newborn. Pregnant inmates who are candidates for vaccination should be evaluated on a case by case basis and counseled regarding the risks and benefits of vaccination during pregnancy.
- All inmate candidates for vaccination should receive counseling on the administration and potential adverse reactions of hepatitis B vaccination by a physician or otherwise qualified health care provider. Counseling, consent, and declination should be documented as per BOP policy.
- The three dose vaccination series is ideally administered at 0, 1, and 6 months, however there is significant flexibility with the administration of the complete series with the following caveats: there must be a 1 month interval between doses #1 and #2; and a 2 month interval between doses #2 and #3; and a 4 month interval between doses #1 and #3. If a dose is delayed the next dose may be administered without restarting the entire series.
- The vaccine is administered intramuscularly in the **deltoid** muscle
- Inmates on chronic hemodialysis or who have anticipated future exposures to HBV infection and are newly vaccinated for hepatitis B, should have anti-HBs levels measured 2 months after the third dose of vaccine. Inmates with subtherapeutic levels of anti-HBs (< 10 mIU) should receive a second three-shot hepatitis B vaccine series with repeat antibody testing 2 months after the third dose of vaccine. If anti-HBs levels

remain subtherapeutic, the inmate should be considered a nonresponder (for the purposes of post-exposure prophylaxis) and monitored for potential acquisition of HBV infection while on dialysis or following known exposures to HBV.

- Periodic serologic testing for anti-HBs in vaccinated inmates is not recommended. Antibody status should be assessed in previously vaccinated inmates after percutaneous or permucosal exposures to assess immunity and the need for further prophylaxis.

Post-exposure management

Inmates with exposures to HBV-infected blood should be counseled by a health care provider regarding the transmission risk, incubation period for acute hepatitis B, the natural history of HBV infection; and the recommendations for post-exposure prophylaxis. Prompt post-exposure prophylaxis with hepatitis B immunoglobulin and/or hepatitis B vaccine should be provided to inmates when indicated in accordance with Appendix 3, Post-exposure Prophylaxis for Hepatitis B Virus, as well as applicable Centers for Disease Control and Prevention (CDC) guidelines.

Hepatitis C

1. Diagnosis

Screening for HCV infection by measurement of anti-HCV by EIA, should be considered for inmates with elevated ALT levels of unknown etiology or signs and symptoms of hepatitis or any of the following:

- History of ever injecting illicit drugs
- Recipient of blood transfusion or organ transplant before 1992
- Recipient of clotting factor transfusion prior to 1987
- History of chronic hemodialysis (screened every 3 to 4 months) unless natural immunity to HCV infection is present
- Percutaneous exposures to HCV-positive blood
- History of tattoos or body piercings received while in jail or prison

Screening for HCV infection in asymptomatic, highly mobile, presentenced inmates in BOP detention facilities should ordinarily not be pursued unless specifically indicated for

medical reasons. Asymptomatic presentenced inmates in BOP detention facilities with histories of injection drug use or other high risk behaviors for HCV infection, should be counseled regarding their risk for HCV infection and behaviors that will reduce transmission of HCV infection to others.

A positive enzyme linked immunoassay (EIA) for HCV antibodies is sufficient to initially diagnose HCV infection in inmates with definitive risk factors for HCV infection and elevations in alanine aminotransferase levels (ALT). A qualitative assay for serum HCV RNA, however, should be obtained for confirmation of infection before initiating antiviral treatment. Inmates with normal ALT levels or no risk factors for HCV infection with a positive EIA for HCV antibodies should have a confirmatory test for HCV infection such as the recombinant immunoblot assay (RIBA™) or a qualitative test for HCV RNA.

2. Natural History (Disease Course)

Acute hepatitis C

The mean incubation period to onset of symptoms after HCV infection is 7 weeks (range 3-20 weeks). Acute hepatitis C is often a mild infection with a self-limited course compared to other forms of acute viral hepatitis. The infection is subclinical in two-thirds of cases. Fulminant acute hepatitis C is rare. The diagnosis of acute viral hepatitis C is based on a positive anti-HCV EIA, and clinical or laboratory evidence of acute hepatitis, without evidence of other viral or noninfectious causes of acute hepatitis. HCV RNA may be detected in the blood 1 to 3 weeks after exposure as an additional test to confirm an acute infection, but viremia may be transient and is unreliable diagnostically. When HCV infection is suspected and the HCV RNA is negative, repeat testing should be considered.

Chronic hepatitis C

An estimated 85% of persons infected with HCV develop chronic hepatitis of varying severity, while 15% of newly infected persons are able to spontaneously clear the virus by unknown mechanisms. HCV viremia and ongoing replication with the development of many HCV quasi-species occurs despite the presence of anti-HCV antibodies. Anti-HCV antibodies do not prevent the progression of liver disease or protect an infected individual from acquiring new HCV infections.

Chronic HCV infection has a waxing and waning course with frequent fluctuations in ALT levels associated with unpredictable degrees of inflammation and fibrosis. Approximately one-third of persons with chronic HCV infection will have subclinical

hepatitis with persistently normal serum ALT levels. Although serum ALT levels do not correlate strongly with histologic progression of disease, persons who develop cirrhosis are more likely to have marked elevations in serum ALT levels. **The strongest predictors for disease progression are a history of heavy alcohol abuse and acquisition of HCV infection after 50 years of age.** An estimated 10% to 20% of persons infected with HCV ultimately develop cirrhosis or clinically significant hepatic disease.

Persons with chronic HCV infection are asymptomatic 80% of the time. Fatigue is the most common presenting complaint, but often symptoms do not become apparent until the infected person has developed cirrhosis and the associated complications of liver failure. HCV infection can be complicated by hepatocellular carcinoma usually in the presence of cirrhosis after longstanding infection of 3 or more decades. Non-hepatic manifestations of HCV infection include essential mixed cryoglobulinemia (frequently presenting as renal failure), membranoproliferative glomerulonephritis, and porphyria cutanea tarda. The presentation of these clinical conditions should prompt evaluation for HCV infection.

3. Monitoring Chronic Infection

A baseline physician evaluation should be conducted for all inmates diagnosed with HCV infection and include at least the following:

- Targeted history and physical examination
- Serum alanine aminotransferase (ALT) levels
- Bilirubin, albumin, prothrombin time and other liver function studies if liver transaminases are elevated
- Renal function assessment
- HBsAg
- HIV serology if risk factors for HIV infection are identified

Periodic clinician evaluations and laboratory studies for inmates with HCV infection should be scheduled and ordered on a case by case basis as clinically indicated depending on the severity of the inmate's liver disease and its associated complications. Inmates with nonelevated ALT levels, or stable marginally elevated ALT levels measured serially over one year, should have ALT levels remeasured every 12 months thereafter. Inmates with

ALT levels greater than 1.5 times normal or with symptoms of hepatitis or other complications should be rescreened and evaluated on a more frequent basis.

Inmates being evaluated for antiviral therapy who have normal liver biopsies should ordinarily be rebiopsied every 4-5 years to reassess for liver inflammation and fibrosis.

Screening tests for hepatocellular cancer have an unclear predictive value and are not routinely indicated. Measurement of serum alpha-fetoprotein levels and a liver ultrasound should be considered for inmates with cirrhosis.

Hepatitis A vaccination should be provided to inmates with hepatitis C and known liver disease, since acute HAV infection may result in a more severe acute hepatitis in this setting. Prescreening for immunity to HAV by screening for HAV IgG, should be considered prior to vaccination.

Hepatitis B co-infection has not been shown to directly exacerbate the liver disease associated with HCV infection, but does complicate antiviral treatment for hepatitis C. Hepatitis B vaccination should be considered for inmates with HCV infection on a case by case basis if the inmate is considered at risk for future infection. Prescreening for immunity to HBV by screening for anti-HBsAg should be considered prior to vaccination.

4. Treatment

Overview of treatment strategies:

Food and Drug Administration-approved regimens with proven efficacy for the treatment of hepatitis C include interferon preparations alone or combination therapy with interferon and ribavirin. **Interferon and ribavirin combination drug therapy is the preferred regimen for treating chronic hepatitis C since it is more efficacious than interferon monotherapy.** Ribavirin is completely ineffective as monotherapy and should never be prescribed without interferon. Interferon monotherapy should ordinarily be considered only when ribavirin is contraindicated. The treatment of hepatitis C should be considered with the complete physician and patient understanding of the following:

- Only 10%-20% of persons with HCV infection develop significant long term complications of liver disease, usually 20-30 years after initial infection. An estimated 3% to 4% of HCV-infected persons will die of complications of their infection.
- No clinical or laboratory parameters definitively predict

which persons infected with HCV will develop cirrhosis or respond to medical therapy. Persons with a history of alcohol abuse are at greater risk of cirrhosis.

- Interferon alpha (3 million units administered subcutaneously 3 times/week for 12 months) alone as initial treatment for HCV infection is approximately 10-25% effective in producing a sustained virologic response. Various formulations for interferon monotherapy have been federally approved for the treatment of hepatitis C. When interferon monotherapy is contemplated (i.e. ribavirin is contraindicated), the treating physician should consult with a physician with expertise in treating hepatitis C to evaluate current efficacy data and determine the optimal formulation and course of treatment.

- Interferon and ribavirin combination therapy is approximately 30%-50% effective in producing a sustained virologic response, but has greater toxicities than interferon alone. **Persons with genotypes 2 or 3 have a 60% to 70% response rate; whereas, persons with genotype 1 have only a 25% to 30% response rate.** Combination interferon/ribavirin is the preferred initial treatment for most inmates who are determined to be candidates for treatment.

Steroids are not an effective treatment for hepatitis C.

Evaluation of inmates for medical treatment of HCV infection should be considered in accordance with Appendix 4 - Evaluation Strategy for Treatment of Hepatitis C. Drug therapy should always be considered with the understanding of the medical contraindications to interferon and ribavirin treatment enumerated in Appendix 2.

Indications/considerations for treatment:

The following medical indications and considerations for antiviral therapy should be used to determine candidates for treatment of hepatitis C:

- Chronic liver inflammation for at least 6-12 months as evidenced by sustained ALT levels 1.5 times greater than normal determined by averaging serum ALT levels on three different occasions measured at least one month apart over 6 - 12 months
- Absence of decompensated cirrhosis: no evidence of signs of end stage liver disease such as ascites, jaundice, esophageal varices or poor liver synthetic function

- Evidence of fibrosis or moderate to severe inflammation on liver biopsy consistent with hepatitis C (HCV causes the following changes in the liver: necrosis and inflammation around portal areas, sometimes referred to as "piecemeal necrosis" or "interface hepatitis", necrosis of hepatocytes and focal inflammation in the liver parenchyma, inflammation of cells in the portal areas, and fibrosis. Fibrosis evolves through the following stages: in the early stages fibrosis is confined to the portal tracts, then in the intermediate stages has greater involvement of the portal tracts with bridging between portal areas or to central areas, and finally to the late stages of frank cirrhosis).
- Absence of absolute contraindications to interferon and ribavirin therapy as enumerated in Appendix 2
- No evidence of active substance abuse (check urine toxicology screen if drug use suspected)
- Careful review of relative contraindications of antiviral therapy

Special treatment considerations

The following special treatment considerations should be assessed when determining the appropriateness of antiviral therapy for hepatitis C:

- Antiviral therapy for hepatitis C should not be prescribed to an inmate who has only recently stopped alcohol or illicit drug use. Typically at least a 6-12 month abstinence is recommended before starting antiviral therapy in nonincarcerated populations. Inmates with histories of substance abuse and hepatitis C should be referred for drug education, nonresidential drug treatment, and residential drug treatment, as appropriate and in accordance with BOP policy as a component of their treatment plan. The timing of antiviral therapy and participation in drug treatment programs should be coordinated on a case by case basis.
- Interferon therapy for persons with hepatitis B and hepatitis C viral co-infections is relatively contraindicated, since safely monitoring the response to treatment and predicting clinical response or deterioration is difficult. Interferon/ribavirin therapy may be considered on a case by case basis in this setting after carefully weighing the benefits and risks of treatment in consultation with a specialist.
- HIV infection may cause chronic hepatitis C to progress more

rapidly to clinically significant liver disease. However, interferon/ribavirin therapy for persons with HIV co-infection or other immunosuppressive conditions is relatively contraindicated, since response rates are unknown and the treatment itself poses an undefined, but real risk of increasing immunosuppression. Inmates with HIV and HCV co-infections should be assessed on a case by case basis with consultations with appropriate subspecialists. Treatment with interferon/ribavirin therapy should only be contemplated for very carefully selected inmates while considering the following:

- Persons with HIV infection should not be treated for hepatitis C with interferon/ribavirin if they are seriously immunocompromised, e.g. CD4 count < 300 cells/mm³.
- Interferon/ribavirin may interact with antiretroviral medications causing serious side effects or weakening the efficacy of the antiretroviral medications. Ribavirin blocks the action of zidovudine (AZT) and stavudine, but other potential drug interactions have not been fully evaluated.
- Since both the benefits and risks of interferon/ribavirin therapy are unknown in this setting, candidates should have definitive evidence of liver disease that poses a significant risk for progression to end stage liver disease, such as moderate or bridging fibrosis on liver biopsy.
- The HCV genotype should be considered in weighing treatment decisions, since genotype significantly predicts the success of treatment
- Antiviral treatment should be considered for persons with chronic HCV infection complicated by mixed essential cryoglobulinemia and renal insufficiency. However, since antiviral therapy may be significantly complicated by renal insufficiency, the decision to treat, as well the specific treatment regimen, should be carefully reviewed with appropriate subspecialists.
- **A negative pregnancy test is essential for women prior to prescribing ribavirin. Furthermore, women of childbearing potential and men must use two forms of effective contraception during treatment and during the six-months post-treatment follow-up period when taking ribavirin.**
- Inmates housed in Federal Detention Centers and Metropolitan Correctional Centers should receive HCV testing as clinically indicated, and comprehensive counseling if found to be

infected. Inmates who are not yet designated, or who are unlikely to remain at their facility for the 12 months of treatment, should not ordinarily be started on interferon/ribavirin; treatment decisions should be deferred until the inmate is sentenced and redesignated to his or her final destination.

Clinical evaluation prior to initiating antiviral therapy for hepatitis C:

Prior to initiating antiviral treatment, inmates who are candidates for treatment should have **qualitative** HCV RNA serologically measured to confirm the presence of HCV infection. Baseline **quantitative** HCV RNA levels are not routinely indicated, are poorly standardized, and therefore should only be measured if needed to specifically help determine treatment strategies. HCV RNA levels are usually considered to be "high" when greater than 2 million copies/mL. High levels of HCV RNA do not correlate with the degree of hepatitis or fibrosis, but are inversely correlated with the likelihood of responding to antiviral therapy. Serial quantitative HCV RNA levels are not indicated.

Inmates with detectable HCV RNA, who are otherwise candidates for antiviral therapy should have a liver/abdominal ultrasound to screen for the presence of other medical conditions that may affect or preclude treatment.

Inmate candidates for antiviral therapy should be referred for subspecialty evaluation and liver biopsy to confirm the diagnosis of hepatitis, preclude other causes of liver disease, grade the severity of injury, assess the degree of fibrosis, and determine the appropriateness of treatment. In situations where a liver biopsy is contraindicated, such as clotting disorders, antiviral therapy should be considered on a case by case basis without a pretreatment liver biopsy.

Inmates should receive the following baseline evaluations/studies (in addition to confirming HCV RNA viremia) prior to considering antiviral therapy:

- Physician evaluation and clearance
- Psychiatrist or psychologist evaluation and clearance
- Serum alanine aminotransferase levels (ALT), albumin, bilirubin, prothrombin time, and creatinine
- CBC with differential and platelet count
- Thyroid function studies (T4/TSH)

- ANA/ferritin
- Serologic assay for HBsAg
- HIV antibody testing
- Pregnancy testing for all female inmates
- Other studies/evaluations to determine the etiology of liver disease as clinically indicated or recommended by subspecialist
- **HCV genotype testing:** HCV genetic diversity is characterized by 6 distinct genotypes, 50 subtypes, and myriad quasi-species. Since persons with genotypes 2 or 3 are almost three times more likely to respond to interferon/ribavirin therapy, genotype testing is important prognostically. Furthermore, genotype testing helps determine the optimal duration of treatment. Genotype 1 is the most common genotype observed in the United States, and predicts a less favorable response to antiviral therapy, however, the decision to prescribe antiviral therapy should never be based solely on the inmate's genotype. The genotype provides information that helps predict treatment success and should be considered by both the physician and the inmate, particularly when relative contraindications exist that may complicate antiviral therapy. Once the HCV genotype has been determined in a specific patient, serial genotype testing is not indicated, since HCV genotypes do not change during the course of an infection. A person with HCV infection can, however, acquire other HCV genotypes if re-exposed to HCV, since host antibodies to HCV do not prevent reinfection.

Administering antiviral therapy for hepatitis C:

Interferon:

Alpha interferon is prescribed as 3 million units by subcutaneous injection thrice weekly when given in combination with ribavirin for treatment of hepatitis C. Treatment with interferon almost universally results in significant side effects. The treating physician should ensure that the inmate is aware of all potential side effects prior to prescribing therapy. An influenza-like reaction usually evolves within 6 - 8 hours of initial treatment with interferon. This acute reaction normally abates with subsequent treatments and can be partially aborted by premedication with antipyretics.

Bone marrow suppression of hematocrit, leukocyte count, and platelet count are serious effects of interferon that should be

anticipated and monitored closely. If bone marrow suppression occurs, interferon should generally be reduced in dosage or discontinued in accordance with Appendix 5, Dosing of Ribavirin and Interferon alpha-2b. Thyroiditis, hyperthyroidism, and hypothyroidism have been reported in 2.5-20% of persons treated with interferon and may result in thyroid dysfunction, even with cessation of drug therapy. Interferon can also induce autoantibodies in an estimated 2% of treated persons after 6 to 12 months of therapy, particularly if underlying illnesses are present such as rheumatoid arthritis or psoriasis. Very serious sequelae of interferon treatment occur in 2% of patients and may include cardiac decompensation, renal failure, pneumonitis, severe bone marrow suppression, and suicide.

Depression, personality changes, and other neuropsychiatric conditions develop commonly with the chronic administration of interferon. In several hepatitis C clinical trials, depression has been the major side effect necessitating the discontinuation of interferon. Inmates who develop signs or symptoms of depression or other neuropsychiatric conditions should be referred to psychology or psychiatry staff for evaluation and possible treatment.

Ribavirin:

Ribavirin is prescribed as 400 mgs (two, 200 mg capsules) taken orally in the morning and 600 mgs (three, 200 mg capsules) taken orally in the evening for persons weighing 75 kg or less; and 600 mgs (three, 200 mg capsules) taken orally in the morning and 600 mgs (three, 200 mg capsules) taken orally in the evening for persons weighing over 75 kg.

Ribavirin causes a dose-related red cell hemolysis to variable degrees in nearly all persons who are treated. A decrease in the hemoglobin of 2 to 3 gm/dL and a decrease in hematocrit of 5% to 10% should be anticipated. Therefore, persons with a preexisting hemolysis or severe anemia (hemoglobin < 11 g or hematocrit < 33%) or underlying cardiovascular or cerebrovascular disease should not receive ribavirin. Anemia ordinarily develops between 1 and 4 weeks of therapy. Symptoms of sudden hemolysis such as dyspnea, fatigue, headache, and palpitations may develop. If anemia occurs ribavirin should be reduced in dosage or discontinued generally in accordance with the guidelines in Appendix 5, Dosing of Ribavirin and Interferon-alpha 2b.

Ribavirin also causes histamine-like side effects such as nasal stuffiness and itching in an estimated 10% to 20% of treated persons. More severe effects can include an asthma-like syndrome or bronchitis.

An unusual but serious complication of interferon or interferon and ribavirin combination therapy is the paradoxical worsening of hepatitis. If ALT levels increase to twice baseline levels, antiviral therapy should be discontinued and ALT levels should be monitored closely and further treatment provided in consultation with a subspecialist.

Monitoring inmates during antiviral treatment:

Serial quantitative HCV RNA assays and serial liver biopsies are **not** routinely indicated for monitoring the response to drug treatment.

Inmates should receive the following evaluations while receiving antiviral therapy for hepatitis C:

- Clinician evaluations before each injection for the first two weeks of treatment and at least biweekly thereafter (Physician evaluations at least monthly)
- Subspecialty evaluations as clinically indicated
- ALT at weeks 1,2, and 4, and at 4-8 week intervals thereafter
- Bilirubin, prothrombin time and other liver function studies with new elevations in ALT
- CBC with differential and platelet count at weeks 1,2, and 4 and at 4-8 week intervals thereafter.
- Thyroid function studies every 3 to 6 months during therapy
- Psychiatry or psychology evaluations as clinically indicated during treatment
- Fundoscopic evaluation for inmates with diabetes or hypertension at baseline, repeated with any complaints of vision problems during treatment
- For inmates receiving interferon/ribavirin treatment measure **qualitative** HCV RNA levels after 24 weeks of treatment and then continue treatment in accordance with the following guidelines:
 - For genotype 1 (1a or 1b), administer treatment for 24 weeks and check HCV RNA. If HCV RNA is undetectable, continue treatment for another 24 weeks (total 12 month

course of treatment). If HCV RNA is still detectable after 24 weeks of interferon/ribavirin, discontinue treatment since this constitutes treatment failure.

- For genotypes 2 and 3, administer treatment for only 24 weeks; at the end of treatment, check HCV RNA to determine if the inmate responded with complete suppression of viral RNA.
- For inmates receiving interferon monotherapy measure HCV RNA at 3 months; if HCV RNA is still detectable and ALT levels remain elevated discontinue interferon therapy.
- After completion of successful interferon or interferon/ribavirin therapy measure ALT levels every 2 months for 6 months
- Measure HCV RNA 6 months after stopping successful therapy; if HCV RNA remains undetectable a sustained response is **probable** with interferon/ribavirin combination therapy and **possible** with interferon monotherapy.

Treatment relapses after interferon monotherapy

Inmates who initially responded to interferon monotherapy and then relapse may be candidates for retreatment with interferon/ribavirin combination therapy, if they have no contraindications to ribavirin. Retreatment should be considered in consultation with a specialist.

Treatment Failures

If an inmate fails to suppress HCV RNA after a recommended course of antiviral treatment with interferon or interferon/ribavirin, regardless of genotype, this constitutes treatment failure. Retreatment with other anti-viral treatment regimens are usually poorly effective, considered investigational, and not ordinarily recommended.

5. Infection control measures

Transmission:

HCV is spread primarily through percutaneous blood exposures such as injection drug use and transfusion of contaminated blood products (prior to effective screening in July, 1992). HCV is inefficiently transmitted through sexual contact, however, persons with a history of sexually transmitted diseases have an increased risk of acquiring HCV infection. HCV can be transmitted from mother to child during pregnancy, but the risk

of transmission is only 5%. Breast-feeding does not transmit HCV from an infected mother to her child. HCV is not spread by sneezing, hugging, coughing, food or water, sharing eating utensils or drinking glasses, or through other casual contact.

All inmates should be counseled during orientation to the institution and when appropriate during clinical evaluations of the importance of preventing blood exposures to others during activities of daily living by not sharing toothbrushes, razors, or other household items that may be contaminated with blood; and by not pursuing prohibited behaviors that may transmit HCV, such as sharing injection drug use equipment, tattooing, and sexual contact with other inmates. All blood exposures from other inmates, regardless of the source, should be considered potentially contagious.

Inmates with known HCV infection should be counseled on the specific measures necessary for preventing further transmission of HCV to others during incarceration and upon release including the following CDC recommendations:

- Do not shoot drugs
- Do not donate blood, body organs, other tissue or semen
- Do not share personal items that might have your blood on them, such as toothbrushes, dental appliances, nail-grooming equipment or razors
- Cover your cuts and skin sores to keep your blood from contacting other persons
- Do not share non-commercial tattooing or body piercing equipment, as the tools and the hands of the tattoo artist can carry infected blood

Inmates with known acute or chronic HCV infection should be managed while incarcerated in accordance with the following guidelines:

- Managed using standard precautions
- Managed using infection control practices in which non-disposable patient-care items are appropriately cleaned, disinfected, or sterilized based on the use; and measures are taken to prevent cross contamination during patient care, i.e., dialysis, vascular access, cauterizing, dental procedures, etc. in accordance with Centers for Disease Control Guidelines on Handwashing and Hospital Environmental Control

- If receiving hemodialysis, anti-HCV positive inmates should be isolated in separate areas and when feasible, assigned units designated for anti-HCV positive inmates only; **or**, scheduled separately for dialysis to prevent cross contamination between seronegative inmates, i.e., anti-HCV positive inmates are dialyzed on different days or time periods than HCV seronegative inmates. In addition, reasonable measures should be taken to provide anti-HCV positive inmates with specifically assigned chairs, medications, supplies, and staff.

6. Post-exposure Management

Inmates with percutaneous or permucosal blood exposures to HCV should be counseled by a qualified health care provider about the transmission, incubation, and natural history of HCV infection in accordance with CDC guidelines. No vaccine, passive immunization, or anti-viral treatments are recommended to prevent or treat newly acquired HCV infection following an exposure. The following guidelines should be used for managing inmate exposures to HCV:

- Whenever feasible, the source of the exposure should be tested for anti-HCV, unless the source's infection status is already known.
- Exposed inmates should be referred for medical evaluation and follow-up.
- Anti-HCV antibodies by EIA (confirmed by RIBA, if positive) and alanine aminotransferase (ALT) levels should be measured at 0 and at 4-6 months following an exposure to screen for newly acquired HCV infection.
- HCV RNA viremia may be measurable 1 to 3 months following an exposure to HCV-infected blood, however, since viremia may be transient, the absence of viremia does not definitively preclude acute HCV infection.
- Inmates with evidence of newly acquired HCV infection should be appropriately counseled and referred for further medical evaluation.

Hepatitis D

1. Diagnosis

Hepatitis D (delta) viral co-infection or superinfection occurs only in the presence of active hepatitis B viral infection (HBsAg+). Inmates at highest risk for delta hepatitis have a

history of injection drug use or have resided in an area of the world with a high prevalence of infection such as Middle East countries, Italy and Central Africa.

Acute Hepatitis D

Acute delta hepatitis can be diagnosed by the presence of anti-HDV IgM, however, this antibody may be present only transiently.

Chronic Hepatitis D

Chronic delta hepatitis can be diagnosed by the presence of anti-HDV IgM and anti-HDV (total). Anti-HDV IgM is a marker for ongoing viral activity/hepatitis. The presence of anti-HDV (total) indicates remote infection with hepatitis D virus, but not necessarily active infection.

2. Disease Course/Monitoring Chronic Infection

Acute delta **co-infection** usually presents as a mild to moderate hepatitis that resolves without development of chronic hepatitis.

Acute delta **superinfection** often presents as a severe hepatitis that resolves, then recurs as chronic delta hepatitis with a rapid progression to cirrhosis and its associated complications.

Periodic clinician evaluations should be conducted for inmates with chronic HDV infection in accordance with guidelines for monitoring chronic hepatitis B. The persistence of chronic delta hepatitis can be assessed by measurement of anti-HDV IgM.

3. Treatment

The treatment of acute delta hepatitis is primarily supportive. Inmates with chronic delta hepatitis should be considered as candidates for interferon therapy using the treatment criteria for managing inmates with chronic HBV infection. The treatment regimen for treating delta hepatitis with interferon, however, differs from the regimens for both hepatitis B and hepatitis C. Treatment should be prescribed and monitored only in consultation with a subspecialist.

4. Infection Control

Hepatitis D virus is transmitted primarily through parenteral blood exposure. Infection control measures applicable for HCV should be utilized for controlling the spread of HDV, including the use of standard precautions for managing infected inmates.

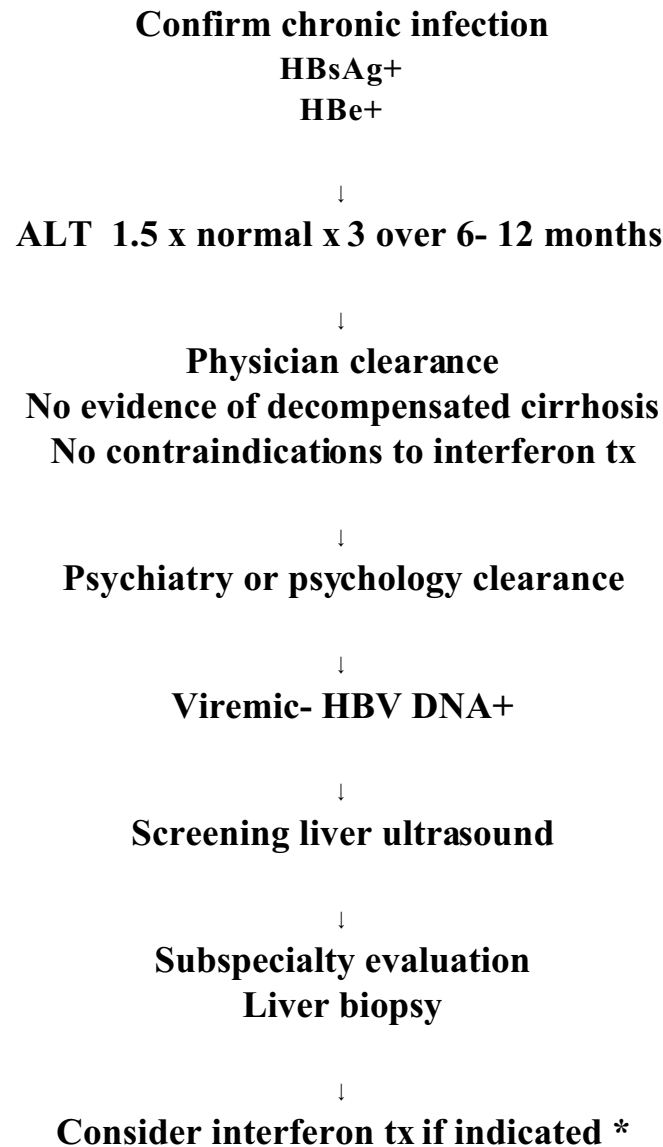
5. Post-exposure Management

Inmates with blood exposures to hepatitis D should be counseled on the transmission, incubation, and natural history of HDV infections. Although no vaccine, passive immunization, or anti-viral treatments are available to specifically abort or treat newly acquired HDV infection, HDV can not newly infect an individual if infection with HBV is prevented with hepatitis B immunoglobulin/hepatitis B vaccine in accordance with CDC guidelines. Contacts who are HBV chronic carriers (HBsAg+) should be counseled on the risk for delta superinfection that can result in severe hepatitis. Inmate contacts should be monitored closely for exacerbations of their liver disease.

ATTACHMENTS

- Appendix 1: Evaluation Strategy for Treatment of Chronic Hepatitis B
- Appendix 2: Contraindications for Interferon and Ribavirin Treatment of Viral Hepatitis
- Appendix 3: Post-exposure Prophylaxis for Hepatitis B
- Appendix 4: Evaluation Strategy for Treatment of Hepatitis C
- Appendix 5: Dosing of Ribavirin/Interferon alpha-2b
- Appendix 6: Resources: Prevention and Treatment of Viral Hepatitis
- Appendix 7: Self-Assessment Review - Viral Hepatitis
- Appendix 8: Self-Assessment Answers - Viral Hepatitis

Evaluation Strategy for Treatment of Chronic Hepatitis B



*Review treatment guidelines for recommendations regarding the use of lamivudine

Contraindications for Interferon or Ribavirin Therapy*

INTERFERON

Absolute Contraindications:

Normal ALT

Decompensated cirrhosis - e.g. albumin < 3, jaundice, ascites, varices, coagulopathy

Hyperthyroidism or hypothyroidism that is uncontrolled

Autoimmune disease that is poorly controlled

Solid organ transplantation

Major depression or other neuropsychiatric condition that is poorly controlled

Active illicit drug or alcohol usage

Relative Contraindications:

Age > 60 years

Bone marrow dysfunction - neutrophils < 1,000/mm³, platelets < 75,000/mm³

History of psychiatric diagnoses

HIV infection

Hepatitis B and C coinfections

Diabetes that is poorly controlled- Hemoglobin A_{1c} > 8.5%

Renal insufficiency; creatinine clearance < 50 mL/min

History of alcohol or substance abuse within the past 6 - 12 months

Cirrhosis of the liver on biopsy without evidence of decompensation

RIBAVIRIN

Absolute contraindications

Pregnancy - due to risk of fetal malformations and fetal death (pregnancy test required prior to initiating therapy; and women of childbearing potential and men must use two forms of effective contraception during treatment and during the six-months post-treatment follow-up period)

Hemoglobinopathies, hemolytic anemias or other severe anemias; with hemoglobin < 11 gm/dL or < 33% hematocrit

Ischemic cardiovascular disease or cerebrovascular disease

Renal insufficiency - creatinine > 2 mg/dL

***Refer to drug manufacturer's warnings in addition to highlighted contraindications**

Post-exposure* Prophylaxis for Hepatitis B Virus[†]

Vaccination Status/Antibody Response	Treatment Based on Source's Hepatitis B Viral Infection Status		
	HBsAg positive	HBsAg negative	Status Unknown
Unvaccinated	HBIG** X 1; Initiate HB vaccine series	Initiate HB vaccine series	Initiate HB vaccine series
Vaccinated - Known Responder***	No treatment	No treatment	No treatment
Vaccinated - Known Non-responder	HBIG X 2; OR HBIG X 1 and revaccination series	No treatment	If known high-risk source, treat as if source were HBsAg positive
Vaccinated - Unknown Response Status	Test exposed person for anti-HBs: If adequate - no treatment If inadequate - HBIG X 1 PLUS vaccine booster	No treatment	Test exposed person for anti-HBs: If adequate - no treatment If inadequate - initiate revaccination

* Exposure is percutaneous (laceration, needlestick, bite) or permucosal (ocular or mucous-membrane) contact with blood.

** Hepatitis B immune globulin (HBIG) dose is 0.06 mL/kg administered intramuscularly at different site than vaccine preferably within 24 hours of exposure; efficacy > 7 days after exposure is unknown.

*** Adequate anti-HBs levels is ≥ 10 mIU/mL.

† Adapted from CDC guidelines, MMWR, Vol. 46, No. RR-18

Evaluation Strategy for Treatment of Chronic Hepatitis C

Diagnose HCV infection

EIA+ - high risk inmate

EIA+/RIBA+ - low risk inmate

↓

Baseline Evaluation

Counseling/examination/basic laboratory studies

↓

Monitor ALT levels for 6 - 12 months

If ALT is persistently 1.5 times normal or greater - pursue further evaluation

↓

Physician Clearance

Assess adherence to previously prescribed treatment plans

Review substance abuse history, particularly injection drug and alcohol use

CBC & differential/platelet count/serum chemistries/liver function studies/creatinine

ANA/TSH/ferritin/pregnancy test/others studies as indicated

Urinalysis toxicology screen for illegal drugs if active substance abuse suspected

Refer to drug treatment program if indicated and available

Review contraindications to interferon/ribavirin therapy

Anticipated incarceration allows for evaluation/completion of treatment

↓

Psychologist or Psychiatrist Clearance

Evaluation for active mental health problems

Rule out major depression or suicidal ideation

Review previous treatment of psychiatric conditions

↓

Confirm Viremia

HCV RNA - qualitative assay; or

HCV RNA - quantitative assay

↓

Liver Ultrasound

Screen for other liver pathology

Rule out ascites

↓

Liver Biopsy/Subspecialty Evaluation

Assess degree of inflammation

Assess degree of fibrosis

Evaluate for co-morbid liver disease

If liver biopsy normal, monitor, rebiopsy in 4-5 years

Subspecialist recommendation

↓

HCV Genotype Determination

↓

Drug Therapy

HCV Genotype 2 or 3 - interferon/ribavirin combination therapy for 24 weeks

**HCV Genotype 1 - interferon/ribavirin therapy - check HCV RNA at 24 weeks
if HCV RNA negative continue for 48 weeks of combination therapy**

**If ribavirin contraindicated, consider interferon monotherapy for 12 months
Discontinue interferon at 3 months if HCV RNA is still detectable and abnormal ALT**

↓

Monitoring Post-treatment

Repeat ALT every 2 months for 6 months after completion of effective therapy

Measure HCV RNA 6 months after completion of effective therapy

Referral to drug treatment program if indicated and not previously completed

DOSING OF RIBAVIRIN/INTERFERON alfa-2b

Recommended Dosing

Body weight	Ribavirin dose	Intron A inj.
75 kg or less	2 X 200mg in AM 3 X 200mg in PM	3 million IU SC 3 times per wk
> 75 kg	3 X 200mg in AM 3 X 200mg in PM	3 million IU SC 3 times per wk

** Ribavirin capsules are limited to pill-line.

Guidelines for Dose Adjustment Based on Hematologic Parameters

Reduce Ribavirin to 600 mg daily (200mg AM, 400mg HS) if:
> Hemoglobin is less than 10 g/dL

Reduce Interferon to 1.5 million units 3 times per week if:
> WBC is less than 1500
> Neutrophil count is less than 750
> Platelet count is less than 50,000

Discontinue treatment (both drugs) if:
> Hemoglobin is less than 8.5 g/dL
> WBC is less than 1000
> Neutrophil count is less than 500
> Platelet count is less than 25,000

For inmates being treated with Interferon/Ribavirin who have a history of cardiac disease (CHF, previous history of MI, angina, or known coronary artery disease by angiography), follow additional recommendations below:

1. Reduce Ribavirin to 600 mg daily (200mg AM, 400mg HS) AND reduce Interferon to 1.5 million units 3 times per week if there is a 2 g/dL drop in hemoglobin during any four week period of treatment.

2. Discontinue Ribavirin and Interferon in cardiac patients if the hemoglobin is less than or equal to 12 g/dL after 4 weeks at the reduced dose (see #1).

Resources: Prevention and Treatment of Viral Hepatitis

Centers for Disease Control and Prevention

1-888-443-7232

(4HEPCDC)

<http://www.cdc.gov/ncid/diseases/hepatitis/index.htm>

*Provides excellent overview of hepatitis C in question and answer format

National Institutes of Health

National Digestive Diseases Information Clearinghouse

<http://www.niddk.nih.gov/health/digest/digest.htm>

1-301-654-3810

*Provides excellent overview of disease management strategies for hepatitis C

American Liver Foundation

1-800-223-0179

(GOLIVER)

1-888-443-7222

(4HEPABC)

Hepatitis Foundation International

1-800-891-0707

<http://www.hepfi.org/>

Self Assessment Review - Viral Hepatitis

Question #1

An inmate presents to your clinic with new onset jaundice, fever, elevated transaminases and normal alkaline phosphatase. You suspect acute viral hepatitis. How should you confirm the diagnosis?

- A. Measure Hep A IgG, HBsAg, and anti-HCV
- B. Measure Hep A IgM, anti-HBc IgM, and anti-HCV
- C. Measure Hep A IgM, anti-HBs, and anti-HCV
- D. Measure Hep A IgM, anti-HBe, and anti-HCV
- E. Measure Hep A IgG, HBsAg, and anti-HCV

Question #2

Which of the following statements is false regarding the transmission of viruses that cause hepatitis?

- A. HAV is spread primarily by fecal-oral contact.
- B. HBV and HCV are spread more easily by percutaneous exposures than HIV.
- C. HCV is not readily transmitted with a single injection of heroin.
- D. HDV can not be acquired without HBV (HBsAg+) infection
- E. HBV infection is a sexually transmitted disease.

Question #3

Which of the following is false regarding HBV infection?

- A. Persons with HBV infection (HBsAg+) and HBe antigen are more contagious than persons with HBsAg+ alone.
- B. Some persons with chronic hepatitis B will spontaneously clear HBV infection (viremia) without treatment.
- C. Antibodies to HBsAg protect a person from new infections.
- D. The presentation of fever, rash, and polyarthrititis is consistent with acute hepatitis B.
- E. Most persons infected with HBV will develop chronic hepatitis.

Question #4

An inmate who is HBsAg+ shares his tattoo needle with 4 other inmates who have never been vaccinated for hepatitis B and all have unknown antibody status (natural immunity) to HBV. Which of the following statements is false regarding the management of the exposed inmates in this setting?

- A. Immediate treatment with hepatitis B immunoglobulin (HBIG) is warranted.
- B. The hepatitis B vaccine series should be initiated concurrently with the HBIG.
- C. Both HBIG and hepatitis B vaccine are indicated for the exposed inmates who are HIV+.
- D. If the exposures occurred 3 months ago HBIG will still be effective in preventing HBV infection.

Question #5

Which of following statements is false regarding the treatment of hepatitis B?

- A. The treatment of acute hepatitis B is primarily supportive.
- B. Inmates with chronic hepatitis B are not candidates for interferon unless they are HBe+.
- C. Interferon is given at lower doses for hepatitis B than for hepatitis C.
- D. Lamivudine monotherapy is an effective treatment for hepatitis B, but its major drawback is the development of HBV resistance.
- E. During effective treatment of hepatitis B and during spontaneous clearance of HBV, the ALT will frequently increase.

Question #6

Which of the following is false regarding testing for HCV infection?

- A. The EIA is a highly sensitive test in diagnosing HCV infection in injection drug users.
- B. Inmates with antibodies to HCV (anti-HCV+) are protected from recurrent infections with HCV.
- C. The RIBA test is helpful in confirming HCV infection for persons at low risk for HCV infection or with normal ALT levels.
- D. Confirming the presence of HCV RNA by qualitative assay is essential before initiating drug therapy for HCV infection.
- E. With acute HCV infection, anti-HCV can be measured with the onset of symptoms in the majority of persons.

Question #7

Which of the following statements is false regarding evaluation of inmates with HCV infection for drug therapy?

- A. Persons with normal ALT levels should ordinarily not be considered for treatment.
- B. A mental health evaluation is essential prior to antiviral therapy, since depression is a serious side effect of interferon.
- C. A liver biopsy should ordinarily be done at baseline prior to initiating drug therapy.
- D. A person with a normal liver biopsy and elevated ALT level is an ideal candidate for interferon and ribavirin.
- E. The specific HCV genotype helps predict response to interferon/ribavirin therapy.

Question #8

Which of the following is false regarding interferon/ribavirin therapy for hepatitis C?

- A. Hemolysis from ribavirin is not dose related.
- B. Ribavirin should never be given as monotherapy.
- C. A flu-like syndrome should be anticipated.
- D. Histamine-like reactions (nasal stuffiness and pruritus) are associated with ribavirin.
- E. Ribavirin causes birth defects.

Question #9

Which of the following statements is false regarding the natural history of hepatitis C?

- A. The HCV viral load helps predict the risk of progression to cirrhosis.
- B. Most persons with hepatitis C will not develop cirrhosis 20 years after their initial infection.
- C. Persons with a history of heavy alcohol use are more likely to develop cirrhosis.
- D. Most persons with hepatitis C have minimal symptoms.

Question #10

Which of the following statements is false regarding antiviral therapy for hepatitis C?

- A. The duration of treatment may be dependent on HCV genotype.
- B. Referral for substance abuse treatment is an important component of the treatment plan for inmates with hepatitis C and injection drug use histories.
- C. Persons have a better response to antiviral treatment if cirrhosis has not developed.
- D. A further elevation in ALT during antiviral therapy usually predicts eventual clearance of HCV viremia.

Self Assessment Answers - Viral Hepatitis

Question #1 - Answer is B

Acute hepatitis A is confirmed by a positive HAV IgM titer that is present during the onset of clinical symptoms. Acute hepatitis B is confirmed by a positive IgM antibody to HBV core antigen (anti-HBc IgM) that develops concurrently with symptoms. The measurement of HBsAg may be clinically helpful, but its presence does not differentiate from acute or chronic HBV infection. Acute hepatitis C is diagnosed by eliminating other causes of viral hepatitis and documenting the presence of anti-HCV antibodies that are present in 60% of patients at the onset of symptoms. HCV RNA, measurable by PCR, may be present during acute HCV infection and can be helpful as a confirmatory test, but a negative test does not preclude acute HCV infection since viremia may be transient.

Question #2 - Answer is C

Hepatitis A virus (HAV) is spread primarily through fecal-oral contact. Hepatitis B virus (HBV) is a sexually transmitted disease that is easily acquired through sexual intercourse. HCV is transmitted through sexual intercourse less efficiently than HBV. Persons with multiple sexual contacts, a history of sexually transmitted diseases, and contacts with prostitutes have a slightly increased risk of HCV infection. HBV, HCV, and HIV, can all be acquired through injection drug use and through occupational exposures to contaminated blood, however, the relative risk of infection differs depending on the type of exposure and the virus. HCV is acquired through injection drug use at rates 79% higher than other bloodborne pathogens such as HBV and HIV. A single experimentation with injection drug use is sufficient to acquire HCV infection. The estimated risk of acquiring a bloodborne pathogen following a single needlestick is 30% for (HBsAg+/HBe+) exposures, 2-4% for HCV exposures, and 0.3% for HIV exposures. Hepatitis D virus, can not infect a person or cause hepatitis without the presence of HBV virus.

Question #3 - Answer is E

Acute hepatitis B may present with fever, rash, and arthritis involving multiple joints. Inmates with a similar presentation should be evaluated for acute HBV infection. Anti-HBs antibodies develop in the majority of persons newly infected with HBV, are usually associated with clearance of HBsAg, and provide long term immunity. Persons infected with HBV who do not develop antibodies are chronically infected (viremic) as evidenced by the

persistence of HBsAg. The presence of HBe in addition to HBsAg indicates increased HBV replication and increased contagiousness. Persons chronically infected with HBV (HBsAg+) can spontaneously clear HBV viremia and develop protective antibodies at a rate of approximately 1%-2% per year. The majority of persons infected with HBV clear their infection and do not develop chronic hepatitis.

Question #4 - Answer is D

Percutaneous exposures to known HBV-contaminated blood in susceptible inmates should be treated in accordance with CDC guidelines by administering HBIG and concurrently initiating the hepatitis B vaccine series (administered at different sites). HBIG is most effective when administered immediately after the exposure; its efficacy more than 7 days after an exposure is unknown. Three months after an exposure to HBV a person will already be infected and HBIG will not abort infection.

Question #5 - Answer is C

The treatment for acute hepatitis B is supportive measures. Persons with chronic hepatitis B are not candidates for treatment unless they are HBe+. Interferon monotherapy and lamivudine monotherapy are FDA-approved treatments for chronic hepatitis B. Lamivudine monotherapy for chronic hepatitis B, although well tolerated and effective, does not prevent the development of resistant HBV strains, and has a high rate of relapse if therapy is discontinued. Interferon is administered in higher doses when treating hepatitis B compared to hepatitis C, therefore side effects may be more prominent. Persons with chronic hepatitis B may experience "flares" of hepatitis from multiple causes, including clearance of the viremia during spontaneous seroconversion or effective antiviral therapy, superinfection with hepatitis D virus, and when administered immunosuppressive medications.

Question #6 - Answer is B

Among inmates with definitive risk factors for HCV infection or increased ALT levels, HCV infection can be adequately diagnosed by measuring anti-HCV by EIA. Inmates without known risk factors for HCV infection or normal ALT levels should have the diagnosis of HCV infection confirmed by measuring anti-HCV by RIBA. The presence of HCV RNA should always be confirmed through a qualitative assay prior to initiating drug therapy for hepatitis C. Acute HCV infection is difficult to diagnose but in 60% of cases anti-HCV by EIA will be measurable at the onset of symptoms and is associated with rising ALT. Antibodies to HCV do not confer immunity. Multiple quasi-species of HCV can exist in the presence of HCV antibodies. Since antibodies are not protective,

reinfection with HCV can also occur and exacerbate underlying disease (e.g. ongoing drug use).

Question #7 - Answer is D

Persons with chronic hepatitis C and normal ALT levels are not ordinarily recommended for interferon/ribavirin treatment, since a beneficial response to treatment is unproven. A mental health evaluation is indicated prior to initiating interferon, since depression and other psychiatric problems occur commonly; and in several large studies depression was the most frequent cause of interrupting antiviral treatment for hepatitis C. A baseline liver biopsy identifies other possible causes of liver disease and assesses the severity of inflammation and fibrosis which are important indicators for treatment. Persons with normal liver biopsies are not candidates for treatment, since the risk of rapid progression to cirrhosis is low and future treatment options may be more effective with less toxicity. Although antiviral treatment decisions should never be made solely on genotype results, the HCV genotype should be considered when weighing treatment options, particularly when relative contraindications to interferon/ribavirin therapy are present. Persons with genotypes 2 or 3 have a 60% - 70% favorable response rate to interferon/ribavirin therapy, compared to persons with genotype 1, who have a much less favorable response rate of 25% to 35%.

Question #8 - Answer is A

A flu-like syndrome should be anticipated 6-8 hours after administering interferon to inmates with hepatitis C. Flu symptoms usually abate with ongoing treatment and can be partially aborted with antipyretics. Ribavirin has no efficacy alone for the treatment of HCV infection. Hemolysis is a dose-related side effect of ribavirin. A drop in hematocrit from hemolysis develops in 10% or more of persons treated with ribavirin usually within weeks of initiating therapy. Moderate decreases in hematocrit can be managed by a dosage reduction of ribavirin. Ribavirin is absolutely contraindicated during pregnancy due to the potential for birth defects and fetal death. Women of childbearing age **and** men must use two forms of effective contraception while taking ribavirin and during the 6 months after treatment has been completed.

Question #9 - Answer is A

The majority of persons with hepatitis C are asymptomatic or have mild symptoms such as slight fatigue. Although persons with HCV infection commonly have minimal to moderate liver inflammation and fibrosis, only 10%-20% of persons with hepatitis C will develop cirrhosis of the liver, usually decades after initial

infection. The greater the HCV RNA levels, the less likely a person will favorably respond to interferon/ribavirin therapy, however, HCV RNA levels do not correlate with the risk for developing cirrhosis. Quantitative HCV RNA levels are not routinely indicated. Heavy daily alcohol use is strongly correlated with the risk of progression to cirrhosis in persons with hepatitis C.

Question #10 - Answer is D

Candidates for interferon/ribavirin therapy should be treated for 24 weeks if they have HCV genotype 2 or 3. Extending treatment beyond 24 weeks is not of further benefit if treatment has not been effective. Inmates with HCV genotype 1 who are treated with interferon/ribavirin therapy and respond to treatment at 24 weeks should have treatment extended to 48 weeks, since the additional 24 weeks of therapy will improve the response rate. A rise in ALT levels during interferon/ribavirin treatment may herald a paradoxical worsening of hepatitis C and warrants discontinuation of antiviral therapy if ALT levels increase significantly. Interferon/ribavirin therapy is contraindicated in persons with decompensated cirrhosis as manifested by poor liver synthetic function and portal hypertension. Inmates with histories of injection drug use and hepatitis C should be referred for drug education, nonresidential drug treatment, or residential drug treatment in accordance with BOP policy. The timing of antiviral therapy when medically indicated, before or after, structured substance abuse treatment programs should be determined on a case by case basis.